Ruptured plaque and TCFA detected by grey-scale and VH-IVUS

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Asan Medical Center, Seoul, Korea
Pathologic Definition of VP

It can not detectable in clinical practice.

Major criteria
- Active inflammation
  (monocyte/macrophage and sometimes T-cell infiltration)
- Thin cap with large lipid core

Practical discrepancy between pathologic definition of VP vs. clinical decision-making in real world
- Stenosis > 90%

Minor criteria
- Superficial calcified nodule
- Glistening yellow
- Intraplaque hemorrhage
- Endothelial dysfunction
- Outward (positive) remodeling

Intermediate lesions at pRCA:

Detection of vulnerable plaque is clinically very important to identify high risk patients before rupture of the plaque occur.
Not vulnerable by angiography and gray-scale IVUS…However, vulnerable by VH-IVUS.
Angiographic Study

One previous study using coronary angiography:

1. 40% of patients with an AMI had multiple complex plaques,

2. These patients had an increased incidence of recurrent ACS, repeat intervention (particularly of non–infarct-related lesions), and CABG in the subsequent year.

Angioscopic study

No. of yellow plaques in a coronary artery

Asakura M. JACC 2001;37: 1284-88
Ruptured Coronary Plaques
IVUS Definition of Plaque Rupture

A plaque with cavity that communicated with the lumen with an overlying residual fibrous cap fragment
IVUS study (n=24)

The only three-vessel IVUS study in ACS patients:

An incidence of culprit lesion plaque rupture: 37.5% (9/24);

Multiple Vulnerable Plaque

At least one secondary (non-culprit) plaque rupture in 79% (19/24) of the patients

IVUS study (n=24 pts)

80% of ACS patients have > 1 ruptured plaque

# ruptured plaques in addition to culprit lesion

Incidence of plaque rupture


<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>AMI (n=122)</th>
<th>SAP (n=113)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRA/ target lesion</td>
<td>80%</td>
<td>66%</td>
</tr>
<tr>
<td>Non-IRA/ non-target lesion</td>
<td>17%</td>
<td>5% *</td>
</tr>
<tr>
<td>Multiple plaque ruptures</td>
<td>20%</td>
<td>6% *</td>
</tr>
</tbody>
</table>

* p<0.01
Total Number of Plaque Rupture

AMI (n=122)

- 60 (49%)

SAP (n=113)

- 28 (25%)
- 18 (15%)
- 6 (5%)
- 4 (3%)
- 0
- 2 (2%)
- 1 (1%)

IVUS in 129 arteries of 45 1st MI patients

Death or ACS-Free Survival

<table>
<thead>
<tr>
<th>Condition</th>
<th>No.</th>
<th>Events Free Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-rupture (n=24)</td>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>Single rupture (n=10)</td>
<td></td>
<td>1.8 (P=0.01)</td>
</tr>
<tr>
<td>Multiple ruptures (n=11)</td>
<td></td>
<td>0.6</td>
</tr>
</tbody>
</table>

P=0.01

Coronary Artery Spatial Distribution of AMI Occlusions

Angiographic analysis in 208 patients

Clustering of Vulnerable Plaque

Location of 273 Plaque Rupture at Coronary Vessels in 158 ACS and 48 SAP

MK Hong et al, J Am Coll Cardiol 2005; 46: 261-265
Long-term Prognosis of Plaque Rupture
Evolution of Spontaneous Atherosclerotic Plaque Rupture With Medical Therapy: Long-Term Follow-Up With IVUS (14 patients, 28 ruptured plaques)

Conclusions—Nearly 2 years of follow-up found that spontaneous coronary atheromatous plaque rupture without significant stenosis detected on first acute coronary syndrome healed without significant plaque modification in 50% of cases with medical therapy. (Rioufol G, et al. Circulation. 2004;110:2875-2880.)
Angioscopic follow-up study of coronary ruptured plaques in nonculprit lesions.

The mean follow-up period was 13 ± 9 months.

The healing rate increased according to the follow-up period (23% at <12 months vs. 55% at >12 months, p = 0.044). The %DS at the healed plaque increased from baseline to follow-up (12.3% to 22.7%, p < 0.05).

The serum CRP level in patients with healed plaques was lower than that in those without healed plaques (p = 0.007).

Takano M et al, J Am Coll Cardiol 2005;45:652–8
## Comparison of three recent studies

<table>
<thead>
<tr>
<th></th>
<th>Rioufol et al</th>
<th>Angioscopy</th>
<th>WHC data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. Patients</strong></td>
<td>14</td>
<td>30</td>
<td>17</td>
</tr>
<tr>
<td><strong>No. Lesions</strong></td>
<td>28</td>
<td>50</td>
<td>17</td>
</tr>
<tr>
<td><strong>F/U duration (months)</strong></td>
<td>22 ± 13 (IVUS FU)</td>
<td>13 ± 9 (angioscopic FU)</td>
<td>43 ± 25 (Clinical FU)</td>
</tr>
<tr>
<td><strong>Healing rate</strong></td>
<td>14/28 lesions (50%)</td>
<td>15/50 lesions (30%)</td>
<td>---------</td>
</tr>
<tr>
<td><strong>Events</strong></td>
<td>No events</td>
<td>1 Rev.</td>
<td>1 death, 2 Rev</td>
</tr>
<tr>
<td><strong>Statin therapy</strong></td>
<td>14 (100%)</td>
<td>Healing (70%), Non-healing (21%)</td>
<td>8 (47%)</td>
</tr>
</tbody>
</table>
Serial intravascular ultrasound evidence of both plaque stabilization and lesion progression in patients with ruptured coronary plaques: effects of statin therapy on ruptured coronary plaque.

Myeong-Ki Hong, Cheol Whan Lee,
Duk-Woo Park, Seung-Whan Lee, Young-Hak Kim,
Jae-Joong Kim, Seong-Wook Park, Seung-Jung Park

Asan Medical Center, Seoul, Korea

Atherosclerosis 2007; 191 :107-114
Study Population

- We identified 28 patients from AMC clinical and IVUS core laboratory database with non-target/non-culprit lesions and without significant stenosis which underwent baseline and 1-year follow-up IVUS study.

- Statin treatment (n=14, 20mg atorvastatin in 7 patients and 40mg simvastatin in 7 patients) vs. non-statin treated group (n=14).
### Clinical outcomes (n=28)

<table>
<thead>
<tr>
<th></th>
<th>Statin (n=14)</th>
<th>No-statin (n=14)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete healing</td>
<td>4</td>
<td>0</td>
<td>0.049</td>
</tr>
<tr>
<td>Incomplete healing</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>No significant changes</td>
<td>10</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Progression to a focal stenosis requiring PCI</td>
<td>0</td>
<td>3</td>
<td>0.11</td>
</tr>
</tbody>
</table>
# Changes in ruptured plaque segment analysis between statin-treated and control lesions.

<table>
<thead>
<tr>
<th></th>
<th>Statin treatment</th>
<th>No-statin group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>∆EEM CSA (mm²)</td>
<td>-0.1±0.1</td>
<td>-0.3±0.7</td>
<td>0.4</td>
</tr>
<tr>
<td>∆Lumen CSA (mm²)</td>
<td>0.4±0.8</td>
<td>-0.6±1.0</td>
<td>0.007</td>
</tr>
<tr>
<td>∆P&amp;M CSA (mm²)</td>
<td>0.0±0.7</td>
<td>0.6±0.9</td>
<td>0.051</td>
</tr>
<tr>
<td>∆Ruptured cavity CSA</td>
<td>-0.5±0.7</td>
<td>-0.3±0.6</td>
<td>0.4</td>
</tr>
<tr>
<td>(mm²)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Changes of ruptured plaque area

- Baseline
  - Control group
  - Statin treatment group

- Follow up
  - Control group
  - Statin treatment group
Conclusion

• The current 12-month follow-up IVUS study showed beneficial effects of statin treatment on reduction of revascularization rates and stabilization of non-culprit/non-target lesion plaque ruptures without significant stenosis.

• Conversely, healing of non-statin-treated non-culprit/non-target lesion plaque ruptures can be responsible for lesion progression requiring revascularization.
Plaque Characterization

Next step →
To identify vulnerable plaque before it rupture and to start statin therapy
New Methodologies to Detect VP

1. MRI
2. Coronary CT
3. Conventional gray-scale IVUS
4. Angiography
5. OCT
6. Thermography
7. VH-IVUS
8. NIR, .....
Virtual Histology™ IVUS

Only the envelope amplitude (echo intensity) is used in formation of the gray-scale IVUS image.

Eight amplitude and frequency parameters are used in Virtual Histology.

Frequency of echo signal can also vary, depending on the tissue.
Comparison of Virtual Histology to Intravascular Ultrasound of Culprit Coronary Lesions in Acute Coronary Syndrome and Target Coronary Lesions in Stable Angina Pectoris

Myeong-Ki Hong, Cheol Whan Lee, Young-Hak Kim, Duk-Woo Park, Seung-Hwan Lee, Jae-Joong Kim, Seong-Wook Park, and Seung-Jung Park

Asan Medical Center, Seoul, Korea

Am J Cardiol 2007: 100; 953-959
Study Populations

• Three hundred eighteen patients who underwent VH-IVUS in the de novo target/ culprit lesions from May 2005 to July 2006.

• Three hundred eighteen patients composed of 195 SAP patients and 123 ACS patients.
Thin-Cap FibroAtheroma (TCFA) by VH-IVUS

- In at least three consecutive frames:
- 1) necrotic core ≥ 10% without evident overlying fibrous tissue and
- 2) percent atheroma area ≥ 40%.

Planar VH-IVUS measurements were performed at 2 lesion segments (minimum lumen cross-sectional area and the largest of necrotic core) and volumetric analysis.
## VH-IVUS in minimum lumen area

<table>
<thead>
<tr>
<th></th>
<th>ACS (n=123)</th>
<th>SAP (n=195)</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Absolute area (mm(^2))</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrotic</td>
<td>5.3±2.7</td>
<td>4.6±3.0</td>
<td>0.030</td>
</tr>
<tr>
<td>Fibrofatty</td>
<td>0.5±0.6</td>
<td>0.5±0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Dense calcium</td>
<td>0.8±0.7</td>
<td>0.6±0.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Necrotic core</td>
<td>3.1±1.9</td>
<td>2.1±1.3</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Percentage (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrotic</td>
<td>53±15</td>
<td>56±15</td>
<td>0.073</td>
</tr>
<tr>
<td>Fibrofatty</td>
<td>5±5</td>
<td>7±6</td>
<td>0.020</td>
</tr>
<tr>
<td>Calcific</td>
<td>9±7</td>
<td>8±8</td>
<td>0.4</td>
</tr>
<tr>
<td>Necrotic</td>
<td>33±14</td>
<td>29±14</td>
<td>0.015</td>
</tr>
</tbody>
</table>

*Cardiovascular Research Foundation*
## VH-IVUS in volumetric analysis

<table>
<thead>
<tr>
<th></th>
<th>ACS (n=123)</th>
<th>SAP (n=195)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Absolute area (mm³)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrotic</td>
<td>41.9±22.4</td>
<td>32.3±20.8</td>
<td>0.001</td>
</tr>
<tr>
<td>Fibrofatty</td>
<td>4.7±4.5</td>
<td>4.5±4.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Dense calcium</td>
<td>6.4±5.1</td>
<td>4.4±4.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Necrotic core</td>
<td>20.3±12.6</td>
<td>14.3±9.5</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Percentage (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrotic</td>
<td>56±13</td>
<td>57±13</td>
<td>0.3</td>
</tr>
<tr>
<td><strong>Fibrofatty</strong></td>
<td>6±5</td>
<td>8±5</td>
<td>0.045</td>
</tr>
<tr>
<td>Calcific</td>
<td>9±7</td>
<td>9±8</td>
<td>0.5</td>
</tr>
<tr>
<td>Necrotic</td>
<td>29±12</td>
<td>27±11</td>
<td>0.081</td>
</tr>
</tbody>
</table>
Ruptured plaque

VH-TCFA

non-VH-TCFA

ACS (n=123) SAP (n=195)

37 15

52 47

38 11

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ANGIOPLASTY SUMMIT
Conclusions

- Compared with SAP patients, plaque CSA was larger in ACS patients because of positive coronary remodeling.
- Larger area of necrotic core and smaller area of fibrotic and fibrofatty plaque were observed in the culprit lesions of ACS patients than in the target lesions of SAP patients.
- Unstable lesions (plaque rupture plus VH-TCFA lesions) were more frequently observed in ACS patients than in SAP patients.
- More data should be gathered to evaluate the efficacy of VH-IVUS examination.
A Patient with Unstable Angina

Single Vessel Disease by Definition
Distal LCX
Proximal LCX
LMCA
A three-vessel virtual histology intravascular ultrasound analysis of frequency and distribution of thin-cap fibroatheromas in patients with acute coronary syndrome and stable angina pectoris.

Myeong-Ki Hong, Cheol Whan Lee, Young-Hak Kim, Duk-Woo Park, Seung-Hwan Lee, Jae-Joong Kim, Seong-Wook Park, and Seung-Jung Park

Asan Medical Center, Seoul, Korea

Am J Cardiol 2008: 101;568-572
Study Populations

- From July 2005 to December 2006, 3-vessel pre-intervention VH-IVUS was attempted in 216 patients at Asan Medical Center. Pre-intervention 3-vessel VH-IVUS was successful in 212 patients (105 with ACS and 107 with SAP) without any complications.

- The ACS group included 47 patients with unstable angina, 22 patients with NSTEMI, and 36 patients with STEMI.
## Total Number of Plaque

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>ACS</th>
<th>SAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruptured plaque</td>
<td>76</td>
<td>55</td>
<td>21</td>
</tr>
<tr>
<td>VH-TCFA</td>
<td>439</td>
<td>262</td>
<td>177</td>
</tr>
<tr>
<td>Non-VH-TCFA</td>
<td>252</td>
<td>75</td>
<td>177</td>
</tr>
</tbody>
</table>
Culprit/target lesions

<table>
<thead>
<tr>
<th></th>
<th>ACS (n=105)</th>
<th>SAP (n=107)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruptured plaque</td>
<td>31</td>
<td>10</td>
</tr>
<tr>
<td>VH-TCFA</td>
<td>61</td>
<td>51</td>
</tr>
<tr>
<td>non-VH-TCFA</td>
<td>9</td>
<td>38</td>
</tr>
</tbody>
</table>

p<0.001, ACS vs. SAP
Non-culprit/non-target lesions

ACS (n=105)  SAP (n=107)

- Ruptured plaque
  - ACS: 8%
  - SAP: 4%

- VH-TCFA
  - ACS: 69%
  - SAP: 45%

- non-VH-TCFA
  - ACS: 23%
  - SAP: 51%

p<0.001, ACS vs. SAP
Average No. of ruptured plaque and VH-TCFA

- ACS
  - Ruptured plaque: 0.5
  - VH-TCFA: 2.5
- SAP
  - Ruptured plaque: 0.2
  - VH-TCFA: 1.7

p<0.001, ACS vs. SAP
Multiple ruptured plaque and VH-TCFA

p<0.001 for ruptured plaque, P=0.009 for VH-TCFA
Frequency distribution of TCFA

ACS (n=105)

SAP (n=107)

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Measured length by VH-IVUS

The total length of the coronary artery imaged by VH-IVUS was

72±16mm in the left anterior descending artery, 
54±12mm in the left circumflex artery, and 
92±19mm in the right coronary artery.
Axial distribution of TCFA and rupture plaque

No. of lesions

Distance (mm) from ostium

- 24% Rupture in ACS (n=55)
- 23% Rupture in SAP (n=21)
- 29% VH-TCFA in ACS (n=262)
- 19% VH-TCFA in SAP (n=177)
Conclusions

- The current 3-vessel VH-IVUS analysis of 212 patients (105 with ACS and 107 with SAP) showed a greater frequency of ruptured plaques, VH-TCFAs, multiple ruptured plaques, and multiple VH-TCFAs in ACS patients compared to SAP patients.

- Ruptured plaques and VH-TCFAs were clustered in the first 40mm of each coronary artery in both ACS and SAP patients.
Thanks for your attention